Serial No. 09/545,334
Group Art Unit: 1638

REMARKS

Claim Rejections – 35 USC §112, First Paragraph - New Matter

Claims 1-4, 7-8, 10, 17, 20-21, 23, 30, 32-33, 35, 42-47, and 60-63 are rejected as failing to comply with the written description requirement with regard to "cytokinin catabolic enzyme", "isogenic", and "maternal tissue."

In order to further prosecution, while reserving the right to pursue unclaimed subject matter in continuation or divisional applications, Claims 1, 17, 30, and 43 have been amended to remove reference to a cytokinin catabolic enzyme, obviating the rejection with respect to these claims and those which are dependent therefrom.

The term "isogenic" appears in the claims in accordance with its usual and customary meaning, i.e., "having the same genotype." (See, e.g., Miglani, Dictionary of Plant Genetics and Molecular Biology, 1998, The Food Products Press, Binghamton, NY) However, in an effort to advance prosecution, Claim 1 has been amended to replace the term . Support for the amendment is found in the specification, for example at page 49 lines 29-35; pages 52, line 26, through page 57, line 15; and Figure 1. The term "nontransgenic siblings" is clear to one of skill in the art.

The term "maternal tissue" has been rejected as new matter. The Applicants respectfully point out that the term "related maternal tissue" appears repeatedly throughout the specification and is defined at page 14.

In light of the amendments and discussion, Applicants ask that all rejections as to new matter be withdrawn.

Claim Rejections – 35 USC §112, Second Paragraph - Indefiniteness

Claims 1-4, 7-8, 10, 13-14, 17, 20-21, 23, 26-27, 30, 32-33, 35, 38-39, 42-47, 49, 53, and 60-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

The metes and bounds of "related maternal tissue" are found to be indefinite. Applicants direct the Examiner's attention to page 2, lines 11-13; page 4, lines 19-21; page 8, lines 5-8; and page 14, lines 17-20.

The metes and bounds of "cytokinin biosynthetic enzyme" are found to be indefinite. Applicants apologize for inadvertently failing to send a copy of the reference offered in the Amendment of July 28, 2003, i.e., Biochemistry & Molecular Biology of Plants (Buchanan, Gruissem & Jones, eds., American Society of Plant Physiologists, Rockville, MD, 2000), particularly pages 874-877, which represents the state of knowledge of cytokinin biosynthesis at the time the application was filed. Applicants include a copy of such pages herewith and submit that the enzymes therein identified as involved in cytokinin biosynthesis comprise "cytokinin biosynthetic enzymes" of the invention. However, in an effort to expedite prosecution in the current application, claims have been amended to recite the cytokinin biosynthetic enzyme isopentenyl transferase.

Claim Rejections – 35 USC §112, First Paragraph – Written Description

Claims 1-4, 7-8, 10, 13, 17, 20-21, 23, 26, 30, 32-33, 35, 38, 42-47, 49, and 60-63 are rejected for not meeting the written description requirement. The Examiner states that the Applicants must disclose "a representative number of cytokinin biosynthetic or cytokinin catabolic enzyme DNA and amino acid sequences or...the structural features common to cytokinin biosynthetic or cytokinin catabolic enzymes."

In an effort to advance prosecution, while reserving the right to pursue unclaimed subject matter in continuation or divisional applications, the claims as amended herein are limited to the cytokinin biosynthetic enzyme isopentenyl transferase.

Claim Rejections – 35 USC §112, First Paragraph – Written Description #2

Claims 1-4, 7-8, 10, 13-14, 17, 20-21, 23, 26-27, 30, 32-33, 35, 38-39, 42-47, 49, 53, and 60-63 stand rejected for inadequate written description. The Examiner states that Applicants have fulfilled the written description requirement for bacterial ipts but not for all ipts, including plant ipts.

In an effort to expedite prosecution, while reserving the right to pursue unclaimed subject matter in continuation or divisional applications, Applicants have amended the claims to encompass only bacterial isopentenyl transferases.

In light of the claim amendments, Applicants respectfully ask that all rejections as to written description be withdrawn.

Claim Rejections – 35 USC §112, First Paragraph – Enablement

Claims 1-4, 7-8, 10, 13, 17, 20-21, 23, 26, 30, 32-33, 35, 38, 42-47, 49, and 60-63 are rejected for failing to meet the enablement requirement. Applicants respectfully traverse the rejection.

The Examiner states that the specification is enabling "for a maize plant transformed with a bacterial isopentenyl transferase encoding polynucleotide (ipt) to produce seeds with increased zeatin levels or expression, increased seed set compared to plants transformed with other genes (page 56, Table 2) and seeds that exhibit vivipary."

New claims 64 and 65 are directed to these embodiments.

The Examiner asserts that the specification is not enabling "for claims drawn to a method of producing a transgenic plant wherein expression of a polynucleotide encoding a cytokinin biosynthetic or cytokinin catabolic enzyme or a plant ipt, is modified; or a transgenic plant, an isolated recombinant DNA molecule, or method for improving stress tolerance and yield stability all of which comprising a cytokinin biosynthetic enzyme, cytokinin catabolic enzyme or a plant ipt encoding nucleic acid." The Examiner states that "undue trial and error experimentation would be

required by one skilled in the art to isolate and screen through the myriad of sequences that are encompassed by Applicants' broad claim language."

Claims 1, 17, 30, 43, and 60-63 have been amended so as to limit the cytokinin biosynthetic enzyme to a bacterial isopentenyl transferase, thus obviating the rejection.

The Examiner further states that the claims are drawn to modifying the expression of a nucleic acid, encompassing both increases and decreases, but that Applicants have only exemplified increasing expression.

Claims 1, 17, 30, 43, and 60-63 have been amended to recite increased expression of a bacterial isopentenyl transferase, thus obviating the rejection.

The Examiner states that Applicants' claimed method for improving stress tolerance and yield stability in plants has not been reduced to practice, and that regulation of the complex processes of stress tolerance and yield stability is unpredictable.

The Applicants respectfully respond that the claimed invention does not, as the Examiner seems to suggest, contemplate isolation of "the gene" encoding the single protein controlling stress tolerance and yield stability. The specification describes use of appropriate combinations of a tissue-preferred, tissue-specific, or temporally-regulated promoter driving expression in developing seeds or related maternal tissue, operably linked to an isolated DNA molecule encoding a cytokinin modulating enzyme, to provide a targeted increase in cytokinin levels leading to improved stress tolerance and yield stability. Applicants also respectfully state that the use of prophetic examples does not automatically make a patent non-enabling. (*Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 224 USPQ409 (Fed. Cir. 1984)) Given the present disclosure, which demonstrates tissue-preferred increase in cytokinin content (see Figure 1), one of skill in the art could make and use the claimed invention.

In light of the amendments and statements made herein, Applicants respectfully ask that the rejections as to enablement be withdrawn.

Serial No. 09/545,334
Group Art Unit: 1638

Claim Rejections – 35 USC §102

Claims 1-2, 4, 13-14, 17, 26-27, 30, 38-39, 42-43, 49, and 53 stand rejected as anticipated by Houck et al. (January 1993, US Patent No. 5,177,307).

"As we have repeatedly stated, anticipation requires that each limitation of a claim must be found in a single reference." *Teleflex, Inc., v. Ficosa North American Corp.*, 209 F.3d 1313, 63 USPQ2d 1374 (Fed. Cir. 2002)

Applicants' previous response pointed out certain distinctions between the cited reference and the present application, including the following:

> "For example, Houck et al. is directed to cytokinin modification so as to increase fruit weight and/or alter the rate of fruit ripening. In contrast, the present application provides utilities of improved seed size, decreased tip kernel abortion and increased seed set during unfavorable environmental conditions (see specification, bottom of p. 4)." (Response 7-28-03, p. 14)

The Examiner states that "the features upon which applicant relies (i.e., utilities of improved seed size, decreased tip kernel abortion and increased seed set during unfavorable environmental conditions) are not recited in the rejected claim(s)."

Claims 1 and 17 have been amended so as to recite the features of interest.

The Examiner states that, as provided in MPEP 2112, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

The Applicants respectfully respond that "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." (MPEP 2112; emphasis in original)

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ 2d 1461, 1464 (BPAI 1990; emphasis in original)

In another case, *In re Robertson*, 169 F.3d 743, 49 USPQ2d 1949 (Fed. Cir. 1999), the Court ruled that the PTO Board erred in holding that a prior art reference (Wilson) anticipated by inherency an applicant's claim. The Board's analysis rested on mere probability or possibility, i.e., that elements in the reference could be used other than as disclosed and for a different function, which is not sufficient to establish inherency. (emphasis added)

It is the Applicants' position that the Examiner has not provided evidence or reasoning tending to show inherency. In addition, the Applicants offer the following evidence that the prior art products do not necessarily possess the characteristics of the claimed product:

1. Increased expression of cytokinin biosynthetic enzyme in seeds did not result in increased yield.

Roeckel, P. *et al.*, (Transgenic Res. 6(2):133-141 (1997)) transformed canola and tobacco with an ipt gene under the control of the developmentally-regulated, seed-specific 2S albumin promoter from Agrobacterium. While ipt mRNA was found only in seeds, and cytokinin levels were evaluated only in seeds, effects of the construct were not limited to seeds; tobacco had reduced roots; canola plants were "surprisingly" (p. 139) taller and had more branches and more seed-bearing structures. However, yield was not affected, nor was leaf type, leaf number, days to first flower, or days to bolting, in either species.

2. Expression targeted to reproductive tissues may have detrimental effects.

Sa et al. (Transgenic Research 11(3):269-278, 2002) reported that transformation of tobacco with *ipt* from *Agrobacterium* under the control of a TA29 promoter, which specifically expresses in anthers, resulted in perturbation in the development of anthers and pollen. About 80% of the T0 transgenic plants exhibited a significant decrease in the rate of pollen germination, and up to 20% of the T0 transgenic plants were male-sterile. In addition, abnormal styles and stamens were found in the transgenic plants.

3. Negative effects resulting from directed expression of transgenic IPT were noted in PCT Publication WO 00/52169:

"These approaches also produce undesirable side-effects in the plant and, even in cases where *ipt* or *rolC* is expressed under the control of tissue-specific promoters, these side-effects are observed in other tissues, presumably because the cytokinin is transported readily between cells and tissues of the plant." (emphasis added)

"That prior art patents may have described failed attempts. . .or attempts that used different elements. . . is not enough. The prior art must be enabling." *Rockwell International Corp. v. United States*, 147 F.3d 1358, 47 USPQ2d 1027 (Fed. Cir. 1998)

In view of the arguments and amendments presented herein, Applicants respectfully ask that all rejections as to anticipation be withdrawn.

Claim Rejections – 35 USC §103

Claims 1-4, 8, 10, 13-14, 17, 21, 23, 26-27,30, 33, 35, 38-39, 42-47,49, and 53 have been rejected under 35 USC 103(a) as unpatentable over Houck et al. (US Patent 5,177,307) in view of Tomes et al. (US Patent 5,877,400).

The Examiner has stated that the 5,177,307 patent "teaches increased cytokinins increase the mass of seeds which improves seed set and increases yield" (OA 12-17-03; referring to column 4, lines 24-27).

Lines 7-31 of Column 4 of the '307 patent are set out below; lines 24-27 are italicized.

> The concentration of cytokinins typically does not remain constant during plant development, and the absolute concentration of the cytokinins in a given tissue may not be dispositive of a physiological effect; rather the cytokinins may act only on tissue rendered competent by other cell factors during a certain phase of development, and/or they may need to be present in concert with other cell factors such as auxins and gibberellins in a particular ratio. Thus, in order to obtain a biological response to the modulated cytokinin concentration, it may be necessary to obtain transcription or expression of the cytokinin gene only at particular stages of interest during development. It will be necessary to identify other cellular products that appear during the period of interest, preferably in the tissue of interest, such as fruit, for example, tomato or cotton roots with respect to auxin/cytokinin "rooting" and *"shooting" ratios in plants, for example, to increase root mass; leaf, for example, tobacco lettuce or petunia; or seeds, for example, rapeseed or soybean; and to demonstrate their absence at other times or in other tissue,* identify nucleic acid sequences associated with the cellular products and then identify the

> sequences in the genome of the plant in order to obtain the 5'untranslated sequences associated with transcription.

Applicants fail to see how these lines establish a teaching that "increased cytokinins increase the mass of seeds which improves seed set and increases yield." The paragraph is directed toward analysis of differential expression of "other cellular products" with a goal of isolation of "5'untranslated sequences associated with transcription" which may be helpful in obtaining "transcription or expression of the cytokinin gene only at particular stages of interest during development."

The Examiner further states that the '307 patent teaches "increased cytokinin levels ameliorate the effects of senescence which can be brought on by stress" (column 3, lines 1-5).

Column 2, line 66, through Column 3, line 5, reads as follows:

> In this manner, cytokinin concentrations can be modulated in a tissue of interest and/or at a period of interest during development of the host plant. Control of cytokinin concentration can be used, for example, to increase solids in fruit and to delay senescence.

This superficial reference to the role of cytokinins in controlling senescence reflects only what was previously known in the art. (See, for example, Thimann, K.V., ed 1980. Senescence in Plants. CRC Press, Inc., Boca Raton, Florida.) It is not an enabling disclosure as to use of an appropriate construct or method to accomplish such control of cytokinin concentration transgenically.

"References relied upon to support a rejection for obviousness must provide an enabling disclosure. That is to say, they must place the claimed invention in the possession of the public." "In order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method." *Beckman Instruments, Inc., v. LKB Produkter AB*, 892 F.2d 1547, 13 USPQ2d 1301 (Fed. Cir. 1989)

Furthermore, the term "senescence" suggests the normal decline and death of a plant following reproductive maturity and does not necessarily connote

environmental stress. In contrast, "stress" as used in the pending application is directed toward unfavorable conditions affecting a much earlier developmental stage:

> These levels act as a metabolic buffer to ameliorate the effects of transient stresses, particularly during the lag phase of seed development, to thus improve corn stress tolerance and yield stability.
>
> It is a further object of this invention to provide a method for improving stress tolerance and yield stability in plants in need thereof, comprising stably introducing into cells of said plants a genetic construct capable of preferentially expressing cytokinin modulating genes during the lag phase of plant seed development, and regenerating and recovering plants from said cells.
> (Both, specification, p. 6)

The Examiner states that the 5,877,400 patent teaches promoters that can be used to express proteins in the embryo and endosperm, that Applicants' arguments are based on the abstract, and that reading the body of the patents teaches the necessary information as discussed above.

The Applicants respectfully respond that the 5,877,400 patent is directed to transgenic methods for producing seedless fruit. In particular it describes use of "a structural gene which promotes the synthesis of or encodes any of the family of gibberellin or gibberellin-like plant hormones." (column 5, lines 50-53) Applicants note only one reference to "promoters that can be used to express proteins in the embryo and endosperm", in Column 10, lines 19-25.

While the Office contends that "the motivation to combine the two patents is presented in both patents, " Applicants fail to find such motivation and ask that the Examiner be specific as to where it appears. Applicants respectfully assert that the combination of '307, directed toward modification of cytokinin to affect fruit ripening, and '400, directed toward modification of gibberellin to produce seedless fruit, would not lead one of skill in the art to constructs and methods for modification of cytokinin to increase seed set and seed yield. "Our case law makes clear that the best defense against hindsight based obviousness analysis is the rigorous application of

the requirement for a showing of a teaching or motivation to combine the prior art references." *Ecolochem, Inc. v. Southern California Edison Co.*, 227 F.3d 1361, 56 USPQ2d 1065 (Fed. Cir. 2000) "[T]he suggestion to combine requirement stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness." *In re Newell*, 891 F.2d 899, 13 USPQ2d 1248 (Fed. Cir. 1989)

In view of the arguments presented herein, Applicants respectfully request that all rejections as to obviousness be withdrawn.

CONCLUSION

Fees for extension of time are provided for in documents accompanying this paper. It is believed that, as there is no net addition of claims, no excess claims fees are due. However, in the event that additional fees are necessary to allow consideration of this paper, such fees, as well as fees for extension of time, are hereby authorized to be charged to Deposit Account # 16-1852 as shown on the enclosed Fee Transmittal.

Applicants believe that all claims under consideration are in condition for allowance, and such action is respectfully requested.

Respectfully submitted,

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